Alterations in Thoracic Duct Lymph Flow in Hepatic Cirrhosis: *

Significance in Portal Hypertension

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LYMPH LEAKING from clusters of bulging lymphatics on the liver capsule and at the porta hepatis often is encountered at laparotomy in patients with Laennec's cirrhosis. This important alteration in hepatic lymph flow, however obscure in origin, apparently initiates ascitic fluid formation. Origin of the other prominent derangement in cirrhosis, elevated portal vein pressure, also is obscure, as is the nature of the relationship between this pressure and bleeding from esophageal varices. To consider that portal hypertension is due to simple portal vein obstruction is to disregard the fact that such hemodynamic effect would be unusual and incapable of experimental duplication.[1,2] Starling pointed out that venous obstruction does not result in sustained venous hypertension.[13] Edema, increased lymph flow and collateral venous flow dissipate the pressure and prevent any significant permanent increase. In the special instance of superior mediastinal syndrome and in constrictive pericarditis sustained venous hypertension is related to failure of dissipation in that lymph formation is so increased that flow through over expanded lymph vessels into obstructed veins is inadequate.[2]

When high protein liver lymph leaks through the liver capsule peritoneal transudation of extracellular fluid is promoted to maintain osmolarity. It is likely that ascites is produced in this manner.[7,8] The relationship between ascites and portal hypertension is not understood, but it may be significant that in patients with hepatic cirrhosis, portal pressures are usually lower in those with massive ascites.[1]

In this report, observations are presented which indicate that inadequate lymph flow in the thoracic duct is implicated in the altered mechanics which result in ascites, portal hypertension and possibly bleeding from esophageal varices. The effects of continuous thoracic duct decompression through an inlying cannula on these features of hepatic cirrhosis are described.

Clinical Observations

Twenty patients were studied. All had evidence of long standing hepatic dysfunction and persistently altered liver function tests. A description of flow and composition of thoracic duct lymph in four of these patients appeared in a preliminary report.[6] The thoracic duct was cannulated in the neck under local anesthesia, with polyethylene or teflon tubes and lymph was allowed to flow freely into suitable collecting vessels. Throughout the period of drainage

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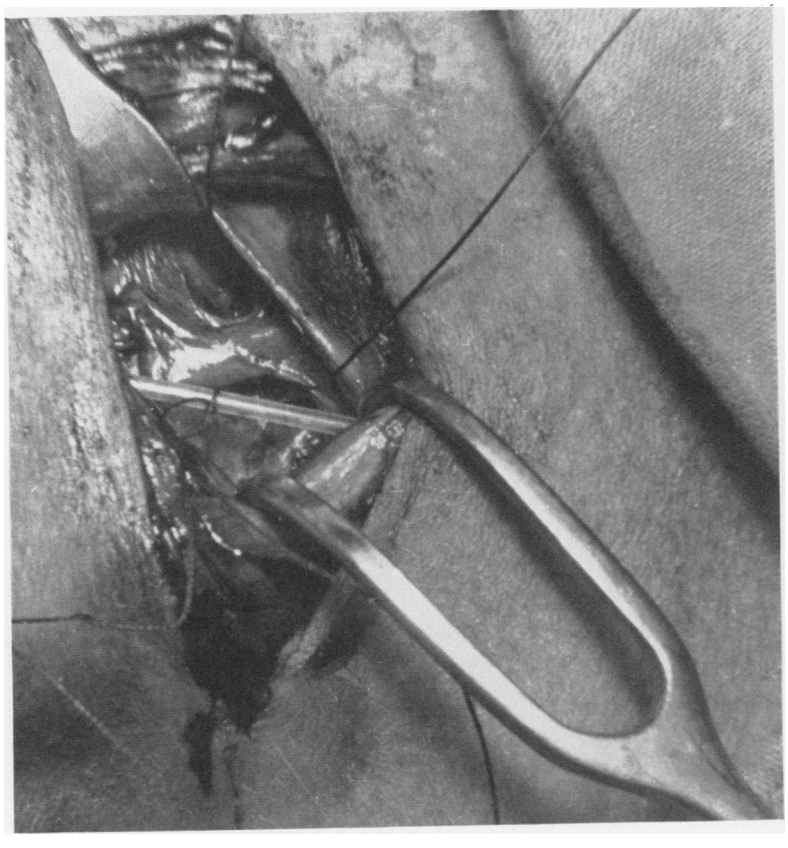

FIG. 1. Dilated thoracic duct in a patient with cirrhosis. A PE 240 plastic cannula has been placed alongside to show comparative size. Normally the thoracic duct is smaller in diameter than the cannula shown here.

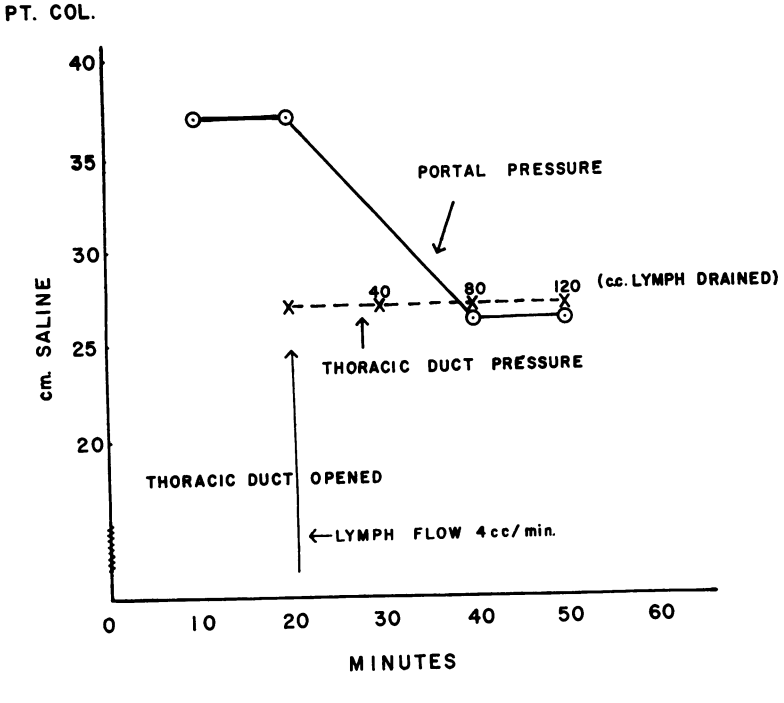

FIG. 2. Rapid decline in splenic pulp pressure following thoracic duct cannulation in a patient with esophageal varices. Thoracic duct pressure remained unchanged.

TABLE 1. *Observations in 20 Consecutive Patients with Hepatic Cirrhosis. End Pressure is Considered to be the Level Above the Duct at Which Flow Through the Cannula Stops*

Patient	Lymph Volume (cm./min.)	Ascites	End Pressure (cm. Saline)		Remarks
			Portal	Lymph	
J. G.	6.0	3+			Varices; ascites disappeared in 6 hours
Mar.	3.0	0	36		Tenfold decreased in flow after portacaval shunt for varices
McC.	6.0	1+	28	26	
Bec.	6.0	0			
Fit.	2.0	3+			Hct. = 8%; flow irregular due to repeated clotting
Fuj.	3.0	1+			Flow irregular due to repeated clotting
Rig.	10.0	1+			Bleeding from varices stopped following cannulation; Hct. = 1%
Hue.	3.0	0	36	23	
Bach.	6.0	2+		25	Hct. = 2%; ascites decreased overnight; splenectomy 1 year before
Toz.	7.0	1+	37	37	Died during portacaval shunt for varices
Cor.	8.0	3+		36 to 58	Hct. = 2%; ascites disappeared overnight; drainage from ascitic fluid fistula ceased in 4 hours
Fri.	12.0	2+		70	Hct. = 1%; bleeding from varices stopped following cannulation
Ega.		2+			Bleeding from varices; coma; huge thoracic duct opened but not cannulated
Her.	2.0	2+			Ascites cleared significantly in 2 days
Mil.	5.0	3+			Hct. = .05%; ascites cleared overnight
Mel.	3.0	2+			Hct. = 21%; cannula removed after 1 hour
Gra.	7.0	3+			Hct. = .5%; ascites cleared overnight
Irv.	2.0	2+			Hct. = 1%; flow stopped shortly after cannulation due to clotting
Ser.		3+			Large thoracic duct opened but not cannulated
Col.	4.0	0	37	27	Hct. = less than 1%; varices

intake of oral and intravenous fluids was adjusted so that significant fluctuations in body weight were avoided. When the cannula was removed and a pressure dressing applied, lymph drainage stopped. No lymph fistulas resulted.

The lymph was invariably hemorrhagic and flowed under pressure from dilated ducts which varied in size within certain limits (Fig. 1). Large channels were found in patients with massive ascites but three of the largest ducts, so large as to be mistaken for the subclavian vein, were found in patients who were bleeding actively from esophageal varices. In two instances, including one of bleeding varices, the cannula could not be introduced because local anatomic conditions created technical difficulties. It was impossible to measure flow rates in these two patients. In the remaining 18 lymph flowed at rates which ranged from 2.0 to 12 cc./min. (normal 1.0 cc. or less per minute—Table 1). In those in whom flow was most rapid a small geyser of lymph shot up when the duct was opened and the duct walls then collapsed.

The hemorrhagic component of the lymph measured as hematocrit, varied from 1.0 to 21 per cent and averaged about 1.0 to 2.0 per cent. In some instances the hematocrit varied 4.0 or 5.0 per cent from hour-to-hour. The red blood cell content of lymph in a dilated duct at times created the appearance of a large blood vessel.

Thoracic duct end pressures were measured in seven patients and ranged from 15 to 70 cm. of saline (normal 6.0–15 cm.). The highest pressure recorded was in a patient who stopped bleeding from esophageal varices following cannulation and in whom lateral pressure in the unopened duct was 49 cm. (normal 4.0–6.0 cm.). End thoracic duct pressures in two patients who had both ascites and varices were 37 and 34 cm. respectively. In a fourth patient flow rate was reduced from 8.0 to 2.0 cc./min. for 24 hours by elevating the end of the cannula. This maneuver increased thoracic duct pressure from 26 to 58 cm. of saline. In another patient with varices, but without ascites, splenic pulp pressure fell from 37 to 26 cm. after the first 20 minutes of lymph drainage. Thoracic duct pressure remained at 27 cm. (Fig. 2).

In four patients the liver was palpable 4.0 to 6.0 cm. below the costal margin. Following cannulation the liver edge grad-

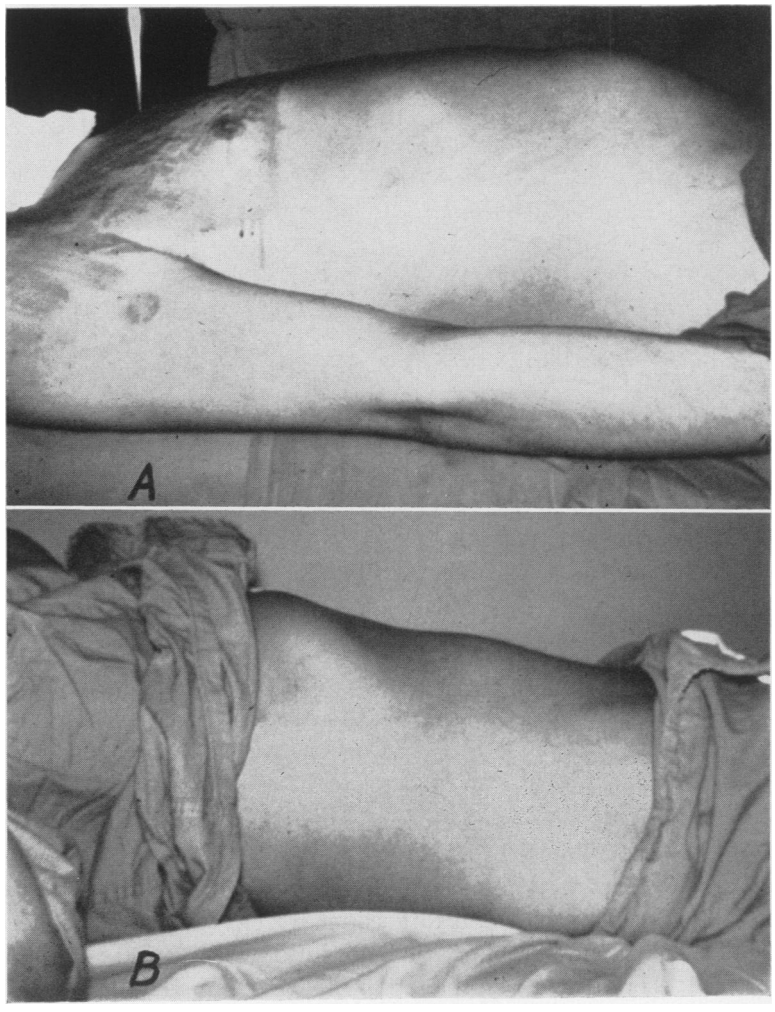

FIG. 3A. Patient with moderate ascites before thoracic duct cannulation. B. Same patient 24 hours after operation.

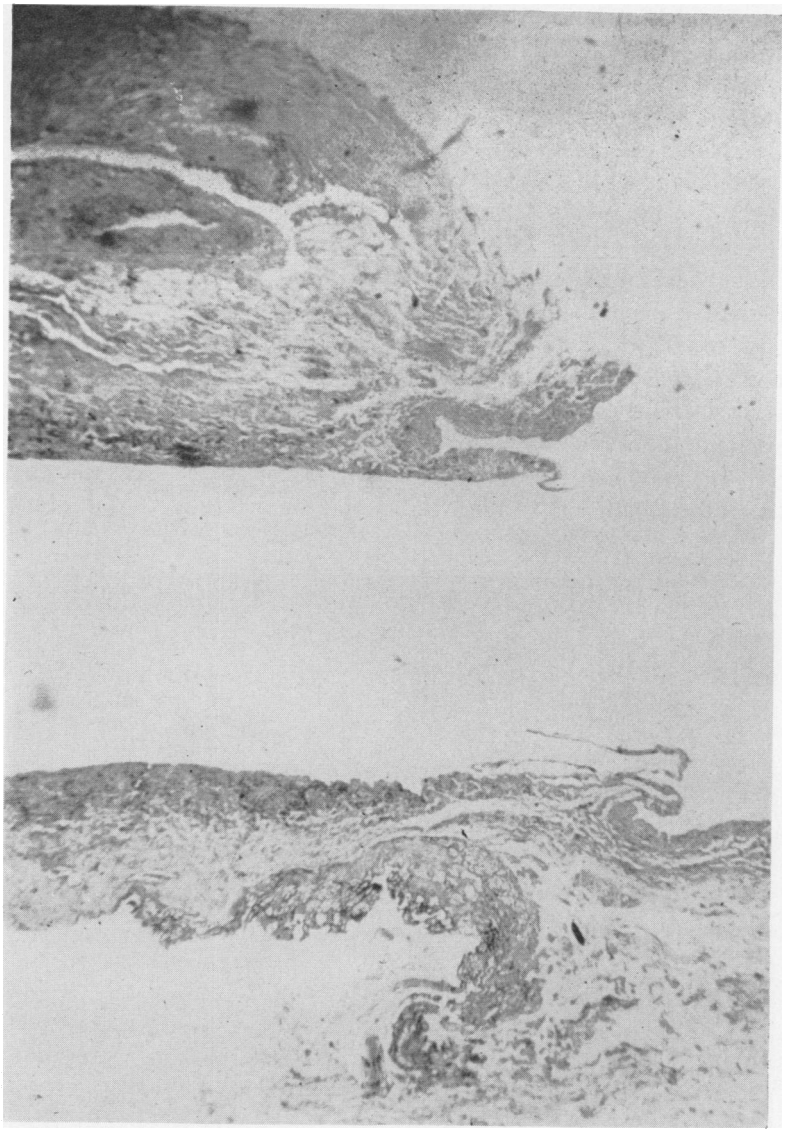

FIG. 4. Photomicrograph showing dilated thoracic duct entering subclavian vein in a patient who died of bleeding esophageal varices. Junction of duct, at the left, with vein is marked by bicuspid valve (from × 60).

ually retreated so that by the time 3.0 to 5.0 liters of lymph had drained the edge was no longer palpable.

In seven patients who had massive ascites the abdomen decreased in size noticeably in five and flattened completely in two (Fig. 3A, B). These changes occurred within 48 to 72 hours, usually by the time 3.0 or 4.0 liters of lymph had been collected, a quantity too small to account for the decrease in amount of ascitic fluid. Mild oliguria accompanied this reduction in size of the abdomen (Fig. 4). In one patient in whom an ascitic fluid fistula in a paracentesis site had been draining for three weeks the fistula closed within four hours of cannulation and drainage ceased permanently. Ascitic fluid reaccumulated gradually following removal of the cannula in all cases.

The duct was cannulated in two patients who were actively bleeding from varices. Both were desperately depleted from protracted blood loss and failing liver function.

Immediately after venting and cannulating the duct, bleeding stopped. In one patient accidental removal of the tube 24 hours later was followed in a few hours by death from massive esophageal bleeding. In the other patient so long as lymph was allowed to flow from the cannula at a rate of 10 to 12 cc./min., no bleeding occurred. On two occasions, attempts to reduce the rate of flow by raising the tip of the cannula were followed by fresh bleeding. On the fifth postoperative day the draining end of the cannula was threaded into a peripheral leg vein to function as a continuous reinfusion. This was an error which actually impeded lymph flow and within two hours massive fatal bleeding ensued.

In five additional patients who had liver diseases other than cirrhosis, both thoracic duct size and rate of flow were normal and the lymph was not hemorrhagic.[5]

Discussion

Increased formation of lymph which contains an abundance of formed blood elements is characteristic of hepatic cirrhosis. These alterations conform with a concept which Krogh proposed 30 years ago: "The normal blood pressure in liver capillaries is extremely low and the flow of lymph is therefore not very great. Any rise in pressure in the liver capillaries will bring about an increase in lymph flow proportional to the pressure and the composition of the lymph will approach so near that of the blood that it must be concluded that the capillaries are permeable to all the blood colloids."[9]

TABLE 2. *Data from Patient G. R. (Fig. 3). Cannula removed at end of 48 hours; 90% of lymph collected was returned to patient by mouth*

		Days			
		1	2	3	4
Weight in pounds		152*	153	155	155
Fluid intake		5,750	3,625	4,045	2,425
Volume in c.c.	Urine	600	1,350	2,625	2,500
	Lymph	4,100	1,700		
Sodium mEq./L.	Urine		16		
	Lymph	141			
	Serum	134		133	
Total protein (Gm./100 ml.)	Lymph	5.9			
	Serum	8.8		7.3	

* Preop. weight.

It is reasonable to speculate that elevated thoracic duct lymph pressure in cirrhosis closely approximates hepatic sinusoidal pressure. Reducing lymph flow by raising resistance at the open end of an implanted cannula significantly increased thoracic duct pressure. Local factors in the neck which limit free flow of excess thoracic duct lmph into the juglo-subclavian junction may therefore influence sinusoidal pressure. The effects of duct cannulation on the duct itself, on bleeding varices, on ascites, on splenic pulp pressure and on liver size must be attributed to free and unimpeded flow of lymph provided by the cannula. It may be assumed, therefore, that free flow from duct to vein was impeded before cannulation. In patients who died from bleeding varices, attempts were made to identify a structural factor which

TABLE 3. *Representative Data Demonstrating Thoracic Duct Lymph and Ascitic Fluid Are Different in Content of Protein, Sodium and Red Blood Cells*

	Serum		Lymph			Ascitic Fluid		
Patient	Total Protein	Na	Total Protein	Na	Appear.	Total Protein	Na	Appear.
M. C. C.	7.3	141	5.4	142	Hem.	1.8	131	Clear
F. I. T.	4.8	156	2.6	170	Hem. c̄ 8% Hct.	1.0	123	Straw Clear

might have limited flow and none was found (Fig. 4). It must be that impedance to flow is the result of an increase in quantity of lymph beyond the capacity of flow channels. When lymph formation is increased the slight but significant resistance normally encountered at the veno-lymphatic junction and the marked distensibility of the thin walled lymphatic channels may combine to bring about insufficient lymph flow. The possibility of relative or *dynamic* insufficiency of hepatic rather than thoracic duct lymph flow in cirrhosis has been considered by Rusznyak.[11] This interpretation does not fit the data reported here.

Venting a distended thoracic duct produced a 10 cm. fall in splenic pulp pressure within 20 minutes. This finding suggests that an important factor in the development of portal hypertension in cirrhosis is the relationship between increased rate of lymph formation and limited rate of flow of thoracic duct lymph into the venous system. It is possible that the effect of thoracic duct cannulation on bleeding from esophageal varices is related to a decrease in portal pressure when adequate lymph flow is established.

After cannulation excess liver lymph flows in the direction of lesser resistance, the thoracic duct, rather than into the peritoneal cavity. Inasmuch as ascitic fluid exchanges with extracellular fluid at the rate of 2.6 l./hr., this could account for disappearance of ascites once liver lymph is diverted.[10] That this disappearance is not direct drainage of ascitic fluid is further indicated by the fact that thoracic duct lymph in cirrhosis differs markedly from ascitic fluid in content of red blood cells and protein (Table 3). Additional evidence regarding the mechanism by which ascites clears has been provided from recent experiments in dogs: ascitic fluid collection following partial constriction of the supradiaphragmatic vena cava can be avoided by shunting thoracic duct lymph into the esophagus, thereby permitting free drainage of excess hepatic lymph.[4] This experiment demonstrates that following hepatic vein outflow obstruction, hepatic lymphatics are capable of transporting excess capillary filtrate, when resistance to thoracic duct flow is removed.

No sustained portal hypertension follows hepatic venous outflow obstruction in dogs.[3] It is likely that the combined effects of increased flow in liver lymphatics, collateral vein formation, escape of excess liver lymph into the peritoneal cavity and liver distension serve to remove a fluid portion of the blood which has been diverted from the vena cava; thus normal portal flow and pressures are maintained.[14]

Portal hypertension has become a convenient clinical expression, although the term implies the presence of information which is in fact lacking. It is curious, for example, the a simple surgical maneuver, performed on a lymphatic in the neck, effects changes usually identified with successful portacaval shunt.

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Discussion

Dr. James D. Hardy (Jackson, Miss.): I did not have an opportunity to see the manuscripts ahead of time, but I believe we have evidence which will reinforce some of the important information which has been described to you.

Dr. Fikri Alican and I have studied various aspects of the thoacic duct, intestinal, and hepatic lymph flow, in some respects paralleling the work of Drs. Dumont and Mulholland.

(slide) May I say, Dr. Litwin and Dr. Cope, that this graph presents data which provide additional evidence that thoracic duct lymph flow does, in fact, increase in hemorrhagic shock. Each one of these cross bars represents a drop of thoracic duct lymph falling into a carefully constructed measuring device, and it may be seen that as the blood pressure of the dog declined following bleeding, there was an increasingly rapid rate of lymph flow.

(slide) This diagram presents endotoxin shock to be compared with the hemorrhagic shock which was previously mentioned. Note that when endotoxin was injected intravenously, there was an initial rise and then a more delayed or secondary rise in the rate of thoracic duct lymph flow. When the portal vein pressure increased, the thoracic lymph flow increased, even though the systemic arterial pressure had usually declined. This initial increase in portal vein pressure and thoracic duct lymph flow following the injection of endotoxin was abolished by portacaval shunt. The more delayed or secondary rise in thoracic duct lymph flow, which usually followed the injection of endotoxin, was not abolished by portacaval shunt and was considered to be due to capillary damage in the splanchnic bed.

(slide) The next slide presents clinical findings in a spectacular case. Operated upon for portal hypertension with esophageal hemorrhage and ascites, this man had an enormous number of lymphatic channels emerging from the hilum of the liver. One of these channels, almost 1.0 cm. in diameter, was ligated and divided to gain acess to the vena cava and the portal vein. Some minutes after it had been ligated, it ruptured spontaneously on the pancreatic side, and lymph spurting several centimeters vertically was easily collected in a specimen cup. This spontaneous rupture due to a build-up in pressure suggested that a similar mechanism may be invoked to explain spontaneous chylothorax which develops in association with malignant tumors. This patient lost from 1.0 to 2.0 liters of lymph into the abdomen during the course of the shunt operation, largely from unnumerable lymphatic vessels of various sizes, with relatively little venous oozing.

(slide) Lastly, the management of a clinical problem will be mentioned. This slide illustrates the procedure used in the operative closure of a thoracic duct fistula which developed in an infant following division of a patent ductus. Using the technic described by Drs. Cohn and Strug, it was the soul of simplicity to inject the Sky Blue dye (Wyeth) into the wall of the esophagus, massage the epigastrium and have the defect in the thoracic duct beautifully delineated. The duct was ligated on both side of the perforation, the lung was decorticated, and the infant whent home in a week. It is recommended that postoperative thoracic duct fistulas be closed by early re-operation, if the chylothorax does not recede within a few days.

Dr. Howard A. Frank (Boston): Dr. Litwin and Dr. Cope were kind enough to show me their plans for these experiments and I wish to express admiration both for the skill in which they were carried out and for the important data they have furnished. The contribution of lymph circulation to the restoration of plasma volume after hemorrhage has received little attention. Dr. Litwin's nicely delivered paper shows us that this neglected mechanism, by restoring plasma protein to circulation, may well be more important than the reabsorption of fluid through the capillary membrane.